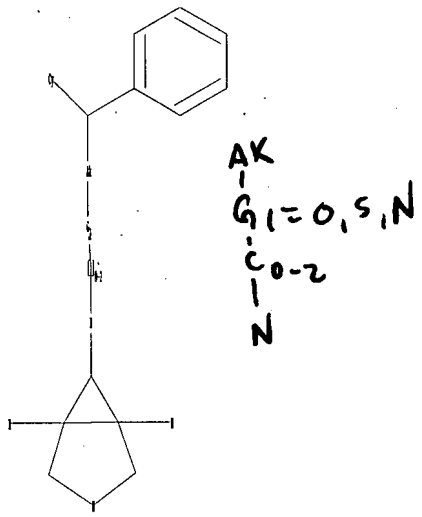
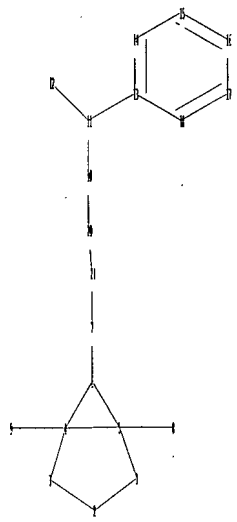




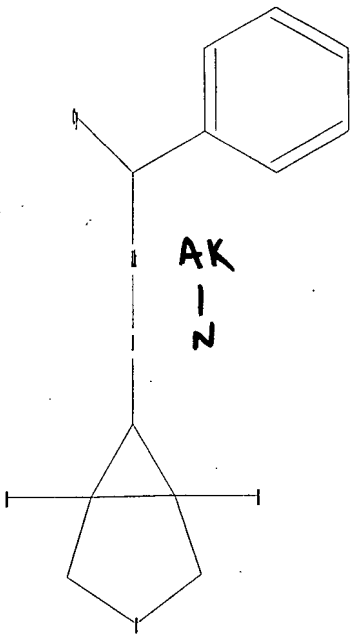
chain nodes :
7 8 9 10 11 12 20 21
ring nodes :
1 2 3 4 5 6 13 14 15 16 17 18
chain bonds :
4-9 5-8 6-7 7-21 10-11 10-20 11-12 11-13 20-21
ring bonds :
1-2 1-5 2-3 3-4 4-5 4-6 5-6 13-14 13-18 14-15 15-16 16-17 17-18
exact/norm bonds :
1-2 1-5 2-3 3-4 4-5 4-6 5-6 6-7 7-21 10-11 10-20 11-12 20-21
exact bonds :
4-9 5-8 11-13
normalized bonds :
13-14 13-18 14-15 15-16 16-17 17-18

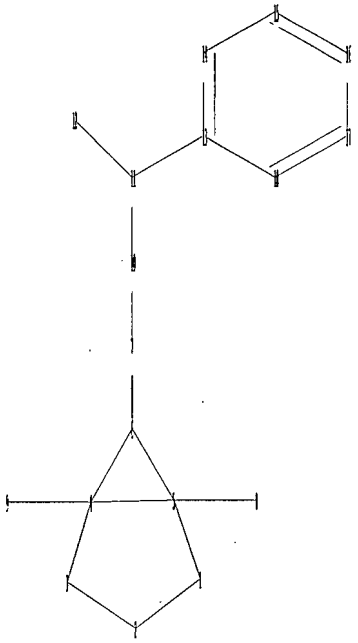
G1:O,S,N

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS
11:CLASS 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 20:CLASS
21:CLASS
Generic attributes :
12:
Saturation : Unsaturated

L1 STRUCTURE UPLOADED

=>
Uploading C:\Program Files\Stnexp\Queries\10552456\1 no O S N.str





chain nodes :
7 8 9 10 11 12
ring nodes :
1 2 3 4 5 6 13 14 15 16 17 18
chain bonds :
4-9 5-8 6-7 7-10 10-11 11-12 11-13
ring bonds :
1-2 1-5 2-3 3-4 4-5 4-6 5-6 13-14 13-18 14-15 15-16 16-17 17-18
exact/norm bonds :
1-2 1-5 2-3 3-4 4-5 4-6 5-6 6-7 7-10 10-11 11-12
exact bonds :
4-9 5-8 11-13
normalized bonds :
13-14 13-18 14-15 15-16 16-17 17-18

Match level :

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1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:CLASS  8:CLASS  9:CLASS  10:CLASS
 11:CLASS  12:Atom  13:Atom  14:Atom  15:Atom  16:Atom  17:Atom  18:Atom
Generic attributes :
12:
Saturation           : Unsaturated



L2      STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1              STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.


=> s l1
SAMPLE SEARCH INITIATED 21:38:35 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -     1447 TO ITERATE

100.0% PROCESSED     1447 ITERATIONS                                 1 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:        26658 TO    31222
PROJECTED ANSWERS:               1 TO       80

L3            1 SEA SSS SAM L1

=> d scan
```

```
=> s l1 full
FULL SEARCH INITIATED 21:39:02 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -     27616 TO ITERATE

100.0% PROCESSED     27616 ITERATIONS                          9 ANSWERS
SEARCH TIME: 00.00.01

L4             9 SEA SSS FUL L1

=> d his

     (FILE 'HOME' ENTERED AT 21:37:38 ON 17 JUN 2007)

     FILE 'REGISTRY' ENTERED AT 21:37:56 ON 17 JUN 2007
L1               STRUCTURE UPLOADED
L2               STRUCTURE UPLOADED
L3             1 S L1
L4             9 S L1 FULL

=> s l2
SAMPLE SEARCH INITIATED 21:39:16 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      3002 TO ITERATE

 66.6% PROCESSED      2000 ITERATIONS                          2 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:        56754 TO    63326
PROJECTED ANSWERS:               2 TO      163

L5             2 SEA SSS SAM L2

=> d scan
```

```
=> s l2 full
FULL SEARCH INITIATED 21:39:35 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED      58234 TO ITERATE

100.0% PROCESSED    58234 ITERATIONS                          35 ANSWERS
SEARCH TIME: 00.00.01

L6            35 SEA SSS FUL L2

=> d his

     (FILE 'HOME' ENTERED AT 21:37:38 ON 17 JUN 2007)

     FILE 'REGISTRY' ENTERED AT 21:37:56 ON 17 JUN 2007
L1               STRUCTURE UPLOADED
L2               STRUCTURE UPLOADED
L3             1 S L1
L4             9 S L1 FULL
L5             2 S L2
L6            35 S L2 FULL

=> fil caplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                               344.65     344.86

FILE 'CAPLUS' ENTERED AT 21:39:48 ON 17 JUN 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)
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FILE COVERS 1907 - 17 Jun 2007  VOL 146 ISS 26
FILE LAST UPDATED: 15 Jun 2007  (20070615/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html

=> s l4 or l6
             3 L4
             8 L6
L7           8 L4 OR L6

=> d ibib abs hitstr 1-8
```

L7 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN

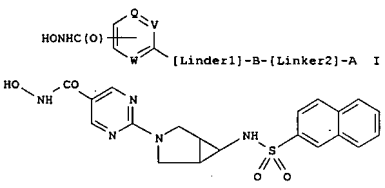
ACCESSION NUMBER: 2006:1226133 CAPLUS
DOCUMENT NUMBER: 145:505473
TITLE: Preparation of hydroxamic acids as histone deacetylase inhibitors for use against proliferative diseases including cancers
INVENTOR(S): Moffat, David Festus Charles; Patel, Sanjay Ratilal; Mazzei, Francesca Ann; Belfield, Andrew James; Van Meurs, Sandra
PATENT ASSIGNEE(S): Chroma Therapeutics Ltd, UK
SOURCE: PCT Int. Appl., 120pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006123121	A1	20061123	WO 2006-GB1779	20060515
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
GB 2429707	A	20070307	GB 2006-18717	20060515

PRIORITY APPLN. INFO.: GB 2005-10204 A 20050519
WO 2006-GB1779 W 20060515

OTHER SOURCE(S): MARPAT 145:505473
GI

L7 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



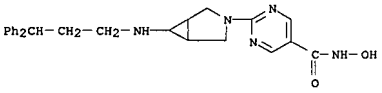
II

AB Hydroxamic acids (shown as I; variables defined below; e.g. N-hydroxy-2-[6-[[(2-naphthyl)sulfonyl]amino]-3-azabicyclo[3.1.0]hex-3-yl]pyrimidine-5-carboxamide hydrochloride (free base shown as II)) and salts, N-oxides, hydrates and solvates thereof are histone deacetylase inhibitors and are useful in the treatment of cell proliferative diseases, including cancers. For I: Q, V and W = N or C; B is a divalent radical = azetidin-1,3-diyl (N on left), 3-azabicyclo[3.1.0]hexane-3,6-diyl (N on either side), hexahydropyrrolo[3,4-c]pyrrole-2,5-diyl and 3,9-diazaspiro[5.5]undecane-3,9-diyl; A is an (un)substituted mono-, bi- or tri-cyclic carbocyclic or heterocyclic ring system; and -[Linker1]- and -[Linker2]- = a bond, or a divalent linker radical; addnl. details are given in the claims. Although the methods of preparation are not claimed, prepns. and/or characterization data for .apprx.80 examples of I are included. For example, II was prepared in 6 steps (82, not given, 85, 93, 87 and 75 % yields, resp.) starting with condensation of tert-Bu 6-amino-3-azabicyclo[3.1.0]hexane-3-carboxylate (preparation given) with 2-naphthalenesulfonyl chloride to give tert-Bu 6-[[(2-naphthyl)sulfonyl]amino]-3-azabicyclo[3.1.0]hexane-3-carboxylate, which was deprotected and alkylated by Et 2-(methylsulfonyl)pyrimidine-5-carboxylate (preparation given) to give Et 2-[6-[[(2-naphthyl)sulfonyl]amino]-3-azabicyclo[3.1.0]hex-3-yl]pyrimidine-5-carboxylate, which was saponified and condensed with O-(1-isobutoxyethyl)hydroxylamine to give N-(1-isobutoxyethoxy)-2-[6-[[(naphthalen-2-yl)sulfonyl]amino]-3-azabicyclo[3.1.0]hex-3-yl]pyrimidine-5-carboxamide, which was cleaved by HCl to give the final product. Semiquant. IC50 values for inhibition of histone deacetylase and U937, HUT and HeLa human cell lines are tabulated for .apprx.80 examples of I.

IT 914937-63-6P, N-Hydroxy-2-[6-(3,3-diphenylpropylamino)-3-azabicyclo[3.1.0]hex-3-yl]pyrimidine-5-carboxamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

L7 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
(drug candidate; prepn. of hydroxamic acids as histone deacetylase inhibitors for use against proliferative diseases including cancers)

RN 914937-63-6 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[6-[(3,3-diphenylpropyl)amino]-3-azabicyclo[3.1.0]hex-3-yl]-N-hydroxy- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

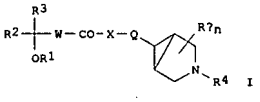
L7 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:1174148 CAPLUS
DOCUMENT NUMBER: 145:471412
TITLE: Preparation of 3,6-disubstituted azabicyclo[3.1.0]hexane derivatives as muscarinic receptor antagonists for use against respiratory, urinary and gastrointestinal diseases
INVENTOR(S): Salman, Mohammad; Kumar, Naresh; Kaur, Kirandeep; Aeron, Shelly; Sarma, Pakala Kumara Savithru; Dharmarajan, Sankaranarayanan; Mehta, Anita; Chugh, Anita
PATENT ASSIGNEE(S): Ranbaxy Laboratories Limited, India
SOURCE: PCT Int. Appl., 79pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006117754	A1	20061109	WO 2006-IB51368	20060501
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRIORITY APPLN. INFO.: IN 2005-DE1810 A 20050503
IN 2006-DE1681 A 20060328

OTHER SOURCE(S): MARPAT 145:471412
GI



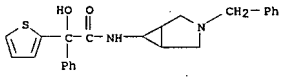
I

AB The present invention generally relates to azabicyclo[3.1.0]hexane derivs. (shown as I; variables defined below; e.g. N-(3-benzyl-3-azabicyclo[3.1.0]hex-6-yl)-2-hydroxy-2-phenyl-2-(2-thienyl)acetamide (1)) as muscarinic receptor antagonists, which are useful, among other uses, for the treatment of various diseases of the respiratory, urinary and gastrointestinal systems mediated through muscarinic receptors. The invention also relates to the process for the preparation of disclosed compds.,

L7 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
pharmaceutical compns. contg. the disclosed compds., and the methods for treating diseases mediated through muscarinic receptors. For I: R1 is H or alkyl; R2 is straight or branched alkyl alkenyl, alkynyl, aryl, cycloalkyl, cycloalkylalkyl or heteroaryl (un)substituted with ≥1 alkyl, hydroxy or halogen. R3 is aryl or heteroaryl (un)substituted with ≥1 alkyl, hydroxy or halogen; W = -(CH2)i; Q = -(CH2)j; X is O or -N(R5)-; R4 is H, straight or branched alkyl, straight or branched alkenyl, aralkyl or heteroarylalkyl wherein the said aralkyl or heteroarylalkyl is further substituted with alkyl, -NH2 or alkoxycarbonylamino; R5 is H or alkyl; RW is H or Me; and n, i, j = 0-2. Results of radioligand binding assays for M2 and M3 muscarinic receptors are reported for many examples of I. Methods of prepn. are claimed and prepns. and/or characterization data for .apprx.120 examples of I are included. For example, 1 was prepd. from hydroxy(phenyl)(thien-2-yl)acetic acid and 3-benzyl-3-azabicyclo[3.1.0]hexan-6-amine in DMF using hydroxybenzotriazole, N-methylmorpholine and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide.

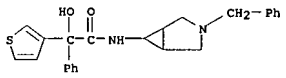
IT 913981-26-7P, N-(3-Benzyl-3-azabicyclo[3.1.0]hex-6-yl)-2-hydroxy-2-phenyl-2-(2-thienyl)acetamide 913981-28-9P, N-(3-Benzyl-3-azabicyclo[3.1.0]hex-6-yl)-2-hydroxy-2-phenyl-2-(3-thienyl)acetamide 913981-36-9P, N-(3-Benzyl-3-azabicyclo[3.1.0]hex-6-yl)-2-(4-fluorophenyl)-2-hydroxy-2-phenylacetamide 913981-37-0P, N-(3-Benzyl-3-azabicyclo[3.1.0]hex-6-yl)-2-hydroxy-2-(4-methylphenyl)-2-phenylacetamide 913981-43-8P, N-(3-Benzyl-3-azabicyclo[3.1.0]hex-6-yl)-2-methoxy-2,2-diphenylacetamide 913981-45-0P, N-(3-Benzyl-3-azabicyclo[3.1.0]hex-6-yl)-N-ethyl-2-hydroxy-2,2-diphenylacetamide 913981-87-0P, N-(3-Azabicyclo[3.1.0]hex-6-yl)-2-methoxy-2,2-diphenylacetamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of 3,6-disubstituted azabicyclo[3.1.0]hexane
derivs. as muscarinic receptor antagonists for use against respiratory,
urinary and gastrointestinal diseases)

RN 913981-26-7 CAPLUS
CN 2-Thiopheneacetamide, α-hydroxy-α-phenyl-N-[3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]- (9CI) (CA INDEX NAME)

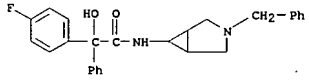


RN 913981-28-9 CAPLUS
CN 3-Thiopheneacetamide, α-hydroxy-α-phenyl-N-[3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]- (9CI) (CA INDEX NAME)

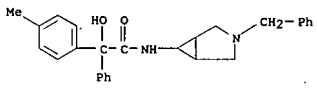
L7 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



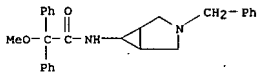
RN 913981-36-9 CAPLUS
CN Benzeneacetamide, 4-fluoro-α-hydroxy-α-phenyl-N-[3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]- (9CI) (CA INDEX NAME)



RN 913981-37-0 CAPLUS
CN Benzeneacetamide, α-hydroxy-4-methyl-α-phenyl-N-[3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]- (9CI) (CA INDEX NAME)

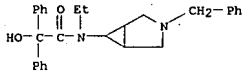


RN 913981-43-8 CAPLUS
CN Benzeneacetamide, α-methoxy-α-phenyl-N-[3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]- (9CI) (CA INDEX NAME)

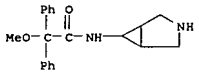


RN 913981-45-0 CAPLUS
CN Benzeneacetamide, N-ethyl-α-hydroxy-α-phenyl-N-[3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]- (9CI) (CA INDEX NAME)

L7 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 913981-87-0 CAPLUS
CN Benzeneacetamide, N-3-azabicyclo[3.1.0]hex-6-yl-α-methoxy-α-phenyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L7 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: ~~2006:1104078~~ CAPLUS
DOCUMENT NUMBER: 146:358692
TITLE: 3,6-Disubstituted azabicyclo[3.1.0]hexane derivatives as muscarinic receptor antagonists, their preparation and use in therapy
INVENTOR(S): Mehta, Anita; Dutt, Silamkoti Viswanatham Arun; Miriyala, Bruhaspathy; Arora, Sudershan Kumar; Srinivasulu, Boju; Mukherjee, Nireshwar; Gupta, Jang Bahadur
PATENT ASSIGNEE(S): Ranbaxy Laboratories Ltd., India
SOURCE: Indian, 63pp.
CODEN: INXXAP
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
IN 193551	A1	20040724	IN 2001-DE1230	20011207
PRIORITY APPLN. INFO.:			IN 2001-DE1230	20011207

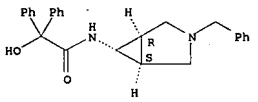
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to azabicyclohexanes of general formula I, which are
muscarinic receptor antagonists. In compds. I, Ar is (un)substituted aryl
or (un)substituted heteroaryl, containing 1 or 2 heteroatoms independently
selected from O, S, and N; R1 is H, OH, halo, CH2OH, NH2, alkoxy, or carbamoyl; R2 is selected from C3-7 cycloalkyl, C3-7 cycloalkenyl, (un)substituted aryl, and (un)substituted heteroaryl, containing 1 or 2 heteroatoms selected from O, S, and N; W is a bond or CH2; X is a bond, O,
S, or N; Y is CH(R5)C(O) or (CH2)q, where R5 is H or Me and q is 0-4; R3 is H, lower alkyl, or CO2CMe3; Z is a bond, CH2, or CH2CH2; and R4 is (un)substituted saturated or unsatd. C1-15 aliphatic hydrocarbon group; including
pharmaceutically acceptable salts thereof. The invention also relates to the preparation of I, pharmaceutical compns. containing compds. of the invention,
as well as to the use of the compns. for the treatment of respiratory, urol., and digestive diseases mediated through muscarinic receptors.
Amidation of (R)-2-cyclopentyl-2-hydroxy-2-phenylacetic acid (reference for
preparation is given) with azabicycle II (reference for preparation is given) gave
carboxamide III, which underwent debenzylating hydrogenation and N-alkylation with 5-bromo-2-methyl-2-pentene to give azabicyclohexane IV. The compds. of the invention are selective muscarinic antagonists, e.g., compound IV expressed 45-fold selectivity for binding to M3 receptors (Ki =
12.4 nM) over M2 receptors (Ki = 564 nM) and expressed KB value of 7.95

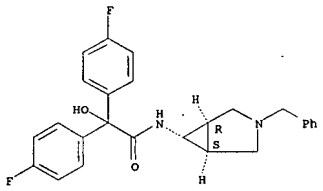
L7 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
in a functional assay.
IT 712355-52-7P 712355-53-8P 712355-54-9P
712355-55-0P 712355-56-1P 712355-57-2P
712355-58-3P 712355-68-5P 712355-69-6P
712355-72-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of azabicyclo[3.1.0]hexane derivs. as muscarinic receptor antagonists)
RN 712355-52-7 CAPLUS
CN Benzeneacetamide, α-hydroxy-α-phenyl-N-[(1α,5α,6α)-3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 712355-53-8 CAPLUS
CN Benzeneacetamide, 4-fluoro-α-(4-fluorophenyl)-α-hydroxy-N-[(1α,5α,6α)-3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]- (9CI) (CA INDEX NAME)

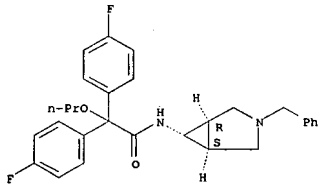
Relative stereochemistry.



RN 712355-54-9 CAPLUS
CN Benzeneacetamide, α-phenyl-N-[(1α,5α,6α)-3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]-α-(2-propenyloxy)- (9CI) (CA INDEX NAME)

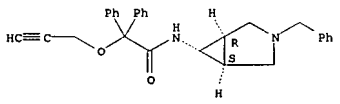
Relative stereochemistry.

L7 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



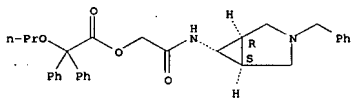
RN 712355-58-3 CAPLUS
CN Benzeneacetamide, α-phenyl-N-[(1α,5α,6α)-3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]-α-(2-propynyloxy)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 712355-68-5 CAPLUS
CN Benzeneacetic acid, α-phenyl-α-propoxy-, 2-oxo-2-[[(1α,5α,6α)-3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]amino]ethyl ester (9CI) (CA INDEX NAME)

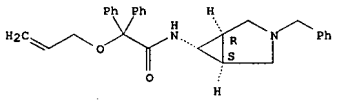
Relative stereochemistry.



RN 712355-69-6 CAPLUS
CN Benzeneacetic acid, α-phenyl-α-(2-propenyloxy)-, 2-oxo-2-[[(1α,5α,6α)-3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]amino]ethyl ester (9CI) (CA INDEX NAME)

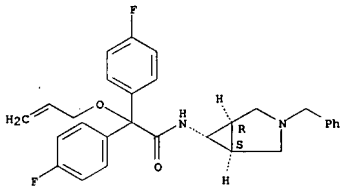
Relative stereochemistry.

L7 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



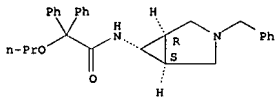
RN 712355-55-0 CAPLUS
CN Benzeneacetamide, 4-fluoro-α-(4-fluorophenyl)-N-[(1α,5α,6α)-3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]-α-(2-propenyloxy)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 712355-56-1 CAPLUS
CN Benzeneacetamide, α-phenyl-N-[(1α,5α,6α)-3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]-α-propoxy- (9CI) (CA INDEX NAME)

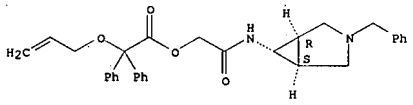
Relative stereochemistry.



RN 712355-57-2 CAPLUS
CN Benzeneacetamide, 4-fluoro-α-(4-fluorophenyl)-N-[(1α,5α,6α)-3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]-α-propoxy- (9CI) (CA INDEX NAME)

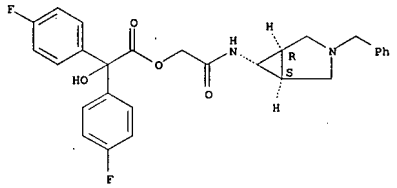
Relative stereochemistry.

L7 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 712355-72-1 CAPLUS
CN Benzeneacetic acid, 4-fluoro-α-(4-fluorophenyl)-α-hydroxy-, 2-oxo-2-[[(1α,5α,6α)-3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]amino]ethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



L7 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:295302 CAPLUS
DOCUMENT NUMBER: 144:350723
TITLE: Preparation of phenyl-substituted amine diols and related compounds as muscarinic receptor antagonists for treating diseases such as those of the respiratory, urinary and gastrointestinal systems
INVENTOR(S): Salman, Mohammad; Sarma, Pakala Kumara Savithru; Dharmarajan, Sankaranarayanan; Chugh, Anita; Gupta, Suman
PATENT ASSIGNEE(S): Ranbaxy Laboratories Limited, India
SOURCE: PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

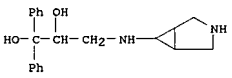
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006032994	A2	20060330	WO 2005-IB2823	20050923
WO 2006032994	A3	20060504		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
EP 1794161	A2	20070613	EP 2005-789768	20050923
R:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR			

PRIORITY APPLN. INFO.: US 2004-613001P P 20040924
WO 2005-IB2823 W 20050923

OTHER SOURCE(S): CASREACT 144:350723; MARPAT 144:350723
AB This present invention generally relates to muscarinic receptor antagonists (PhC(X)(OH)C(:G)CH2N(R1)(R2) (I) or PhC(X)(OH)C(G)CH2N(R1)(R2) (II); variables defined below; e.g. 1-cyclopentyl-3-([1,4]diazepan-1-yl)-1-hydroxy-1-phenylpropan-2-one), which are useful, among other uses, for the treatment of various diseases of the respiratory, urinary and gastrointestinal systems mediated through muscarinic receptors. The invention also relates to the process for the preparation of disclosed compds., pharmaceutical compns. containing the disclosed compds., and the methods for treating diseases mediated through muscarinic receptors. For I and II: X = alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, heterocyclyl, heterocyclylalkyl, or heteroarylalkyl; R1 = H, alkyl, alkenyl, alkynyl, cycloalkyl, alkoxy, aryloxy, -(CH2)0-2-heterocyclylalkyl, or -(CH2)0-2-heteroarylalkyl; R2 = -(CH2)0-2-heteroaryl, -(CH2)0-2-heterocyclyl, or -(CH2)0-2-aryl, or R1 and R2 may together combine to form a (un)satd. monocyclic or bicyclic ring system contg. 0-4 heteroatoms (O, N or S) wherein the ring can be (un)substituted with ≥1 of alkyl, alkenyl, alkynyl, cycloalkyl, alkaryl, alkoxy, aryloxy, et al.; G = -OR [R = H or unsubstituted lower (C1-C6) alkyl], -NOR, -NHYR' (R' is H, alkyl or aryl and Y is -C(O), -SO or -SO2), or O (provided that R1 and R2 together does not form a pyrrolidine, 4-hydroxypiperidine, 4-pyrrolidinylpiperidine, piperazine or azabicyclo[3.1.0]hexane ring). Methods of prepn. are claimed and prepns. and/or characterization data for .apprx.80 examples of I are included. For example, 1-cyclopentyl-1-hydroxy-1-phenyl-3-(piperidin-1-yl)propan-2-one was prepd. (86 %) from piperidine, Et3N and 3-bromo-1-cyclopentyl-1-hydroxy-1-phenyl-2-propanone (prepn. described) in CH2Cl2. Ki values for I tested in a radioligand binding assay range from .apprx.5 nM to .apprx.10 μM for M2 receptors, and from .apprx.0.5 nM to .apprx.10 μM for M3 receptors. Selectivity for bladder pressure inhibition vs. salivation was detd. for compd. 3 examples of I and was .apprx.2, similar to that detd. for tolterodine.

IT 881098-67-5P, 3-[(3-Azabicyclo[3.1.0]hex-6-yl)amino]-1,1-diphenylpropane-1,2-diol 881098-77-7P 881206-00-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of Ph-substituted amine diols and related compds. as muscarinic receptor antagonists for treating diseases such as those of respiratory, urinary and gastrointestinal systems)

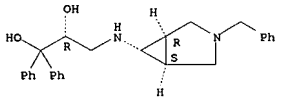
RN 881098-67-5 CAPLUS
CN 1,2-Propanediol, 3-(3-azabicyclo[3.1.0]hex-6-ylamino)-1,1-diphenyl- (9CI) (CA INDEX NAME)



RN 881098-77-7 CAPLUS
CN 1,2-Propanediol, 1,1-diphenyl-3-[{(1α,5α,6α)-3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl}amino]-, (2R)- (9CI) (CA INDEX NAME)

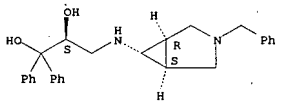
Absolute stereochemistry.

L7 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 881206-00-4 CAPLUS
CN 1,2-Propanediol, 1,1-diphenyl-3-[{(1α,5α,6α)-3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl}amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L7 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:872781 CAPLUS
DOCUMENT NUMBER: 141:350045
TITLE: Preparation of substituted azabicyclo hexane derivatives as muscarinic receptor antagonists
INVENTOR(S): Mehta, Anita; Miriyala, Bruhaspathy; Arora, Sudershan Kumar; Gupta, Jang Bahadur
PATENT ASSIGNEE(S): Ranbaxy Laboratories Limited, India
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004089898	A1	20041021	WO 2003-IB1288	20030409
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU 2003214520	A1	20041101	AU 2003-214520	20030409
EP 1618091	A1	20060125	EP 2003-710099	20030409
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
US 2006281805	A1	20061214	US 2006-552456	20060814

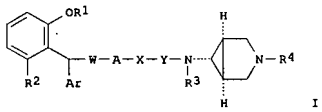
PRIORITY APPLN. INFO.: WO 2003-IB1288 A 20030409

OTHER SOURCE(S): MARPAT 141:350045
GI

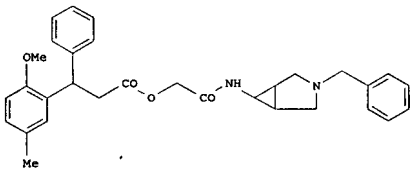
Instant App.

10/552456

L7 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



I



II

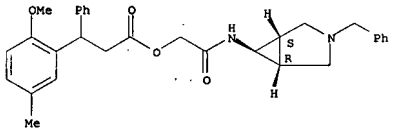
AB Title compds. I [Ar = (hetero)aryl, etc.; R1 = H, alk(en/yn)yl, etc.; R2 = H, alkyl; A = (CH2)0-4, CO; W = (CH2)1-4; X = O, S, amino; Y = alkyl; R3-4 = H, alkyl, cycloalkyl, etc.] are prepared For instance, II is prepared from (3-benzyl-3-azabicyclo[3.1.0]hexan-6-yl)amine, 2-chloroacetyl chloride and (2-methoxy-5-methylphenyl)-3-phenylpropanoic acid. II exhibited pKi < 6 for both the muscarinic M2 and M3 receptors. I are useful for the treatment of respiratory, urinary and gastrointestinal disorders.

IT 777068-38-9P 777068-40-3P 777068-58-3P
777068-64-1P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of substituted azabicyclo hexane derivs. as muscarinic M2 and M3 receptor antagonists)

RN 777068-38-9 CAPLUS
CN Benzenepropanoic acid, 2-methoxy-5-methyl-β-phenyl-, 2-oxo-2-[[(1α,5α,6α)-3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]amino]ethyl ester (9CI) (CA INDEX NAME)

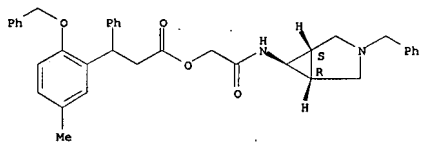
Relative stereochemistry.

L7 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



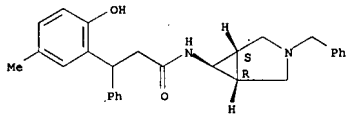
RN 777068-40-3 CAPLUS
CN Benzenepropanoic acid, 5-methyl-β-phenyl-2-(phenylmethoxy)-, 2-oxo-2-[[(1α,5α,6α)-3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]amino]ethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 777068-58-3 CAPLUS
CN Benzenepropanamide, 2-hydroxy-5-methyl-β-phenyl-N-[(1α,5α,6α)-3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]- (9CI) (CA INDEX NAME)

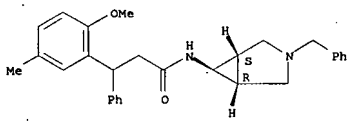
Relative stereochemistry.



RN 777068-64-1 CAPLUS
CN Benzenepropanamide, 2-methoxy-5-methyl-β-phenyl-N-[(1α,5α,6α)-3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

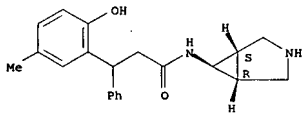
L7 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



IT 777068-42-5P 777068-44-7P 777068-50-5P
777068-52-7P 777068-55-0P 777068-57-2P
777068-66-3P 777068-67-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted azabicyclo hexane derivs. as muscarinic M2 and M3 receptor antagonists)

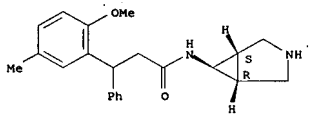
RN 777068-42-5 CAPLUS
CN Benzenepropanamide, N-(1α,5α,6α)-3-azabicyclo[3.1.0]hex-6-yl-2-hydroxy-5-methyl-β-phenyl- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 777068-44-7 CAPLUS
CN Benzenepropanamide, N-(1α,5α,6α)-3-azabicyclo[3.1.0]hex-6-yl-2-methoxy-5-methyl-β-phenyl- (9CI) (CA INDEX NAME)

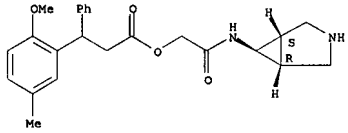
Relative stereochemistry.



RN 777068-50-5 CAPLUS
CN Benzenepropanoic acid, 2-methoxy-5-methyl-β-phenyl-, 2-[(1α,5α,6α)-3-azabicyclo[3.1.0]hex-6-ylamino]-2-oxoethyl ester (9CI) (CA INDEX NAME)

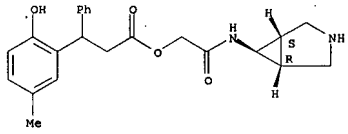
Relative stereochemistry.

L7 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



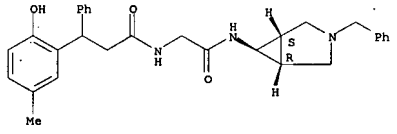
RN 777068-52-7 CAPLUS
CN Benzenepropanoic acid, 2-hydroxy-5-methyl-β-phenyl-, 2-[(1α,5α,6α)-3-azabicyclo[3.1.0]hex-6-ylamino]-2-oxoethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 777068-55-0 CAPLUS
CN Benzenepropanamide, 2-hydroxy-5-methyl-N-[2-oxo-2-[[(1α,5α,6α)-3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]amino]ethyl]-β-phenyl- (9CI) (CA INDEX NAME)

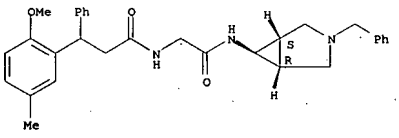
Relative stereochemistry.



RN 777068-57-2 CAPLUS
CN Benzenepropanamide, 2-methoxy-5-methyl-N-[2-oxo-2-[[(1α,5α,6α)-3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]amino]ethyl]-β-phenyl- (9CI) (CA INDEX NAME)

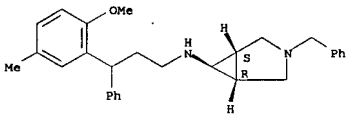
Relative stereochemistry.

L7 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



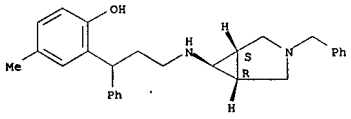
RN 777068-66-3 CAPLUS
CN 3-Azabicyclo[3.1.0]hexan-6-amine, N-[3-(2-methoxy-5-methylphenyl)-3-phenylpropyl]-3-(phenylmethyl)-, (1α,5α,6α)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 777068-67-4 CAPLUS
CN Phenol, 4-methyl-2-[1-phenyl-3-[[(1α,5α,6α)-3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]amino]propyl]- (9CI) (CA INDEX NAME)

Relative stereochemistry.



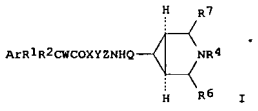
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L7 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:675748 CAPLUS
DOCUMENT NUMBER: 141:207060
TITLE: Preparation of azabicyclo[3.1.0]hexanes as muscarinic receptor antagonists
INVENTOR(S): Mehta, Anita; Miriyala, Bruhaspathy; Kumar, Naresh; Gupta, Jang Bahadur
PATENT ASSIGNEE(S): Ranbaxy Laboratories Limited, India
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004069835	A1	20040819	WO 2003-IB416	20030207
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003205964	A1	20040830	AU 2003-205964	20030207
EP 1594871	A1	20051116	EP 2003-702847	20030207
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2007010568	A1	20070111	US 2006-544520	20060904
PRIORITY APPLN. INFO.:			WO 2003-IB416 A	20030207

OTHER SOURCE(S): CASREACT 141:207060; MARPAT 141:207060
GI

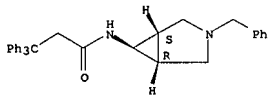


AB Title compds. [I; Ar = (substituted) aryl, heteroaryl; R1 = H, OH, HOCH2, aryl, alkylaryl, amino, alkoxy, carbamoyl, halo; R2 = alkyl, cycloalkyl cycloalkenyl, (substituted) aryl, heteroaryl; W = (CH2)p; p = 0, 1; X = O, S, NR, null; Y = null, CHR5CO, Me, (CH2)q; q = 0-4; R5 = H; Z = null,

10/544520
17 Claims

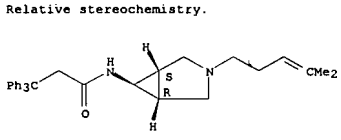
L7 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
NHR8CO; R8 = (CH2)r; r = 0-4; Q = (CH2)n; n = 0, 1; R6, R7 = H, Me, CO2H, CONH2, NH2, CH2NH2; R4 = H, (substituted) (unsatd.) hydrocarbyl], were prepd. Thus, N-[(1α,5α,6α)-3-azabicyclo[3.1.0]hexan-6-yl] 3,3,3-triphenylpropionamide, 4-methyl-3-pentenyl bromide, K2CO3, and KI were stirred in DMF at 60-70° for 3 h and at room temp. overnight to give N-[(1α,5α,6α)-3-(4-methyl-3-pentenyl)azabicyclo[3.1.0]hexan-6-yl] 3,3,3-triphenylpropionamide. I bound to M2 and M3 receptors with pKi <6.
IT 741676-03-9P 741676-04-0P 741676-05-1P
741676-06-2P 741676-09-5P 741676-10-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(claimed compound; preparation of azabicyclohexanes as muscarinic receptor antagonists)
RN 741676-03-9 CAPLUS
CN Benzenepropanamide, β,β-diphenyl-N-[(1α,5α,6α)-3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 741676-04-0 CAPLUS
CN Benzenepropanamide, N-[(1α,5α,6α)-3-(4-methyl-3-pentenyl)-3-azabicyclo[3.1.0]hex-6-yl]-β,β-diphenyl- (9CI) (CA INDEX NAME)

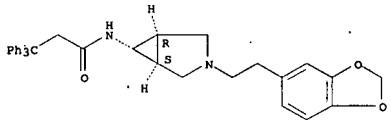
Relative stereochemistry.



RN 741676-05-1 CAPLUS
CN Benzenepropanamide, N-[(1α,5α,6α)-3-[2-(1,3-benzodioxol-5-yl)ethyl]-3-azabicyclo[3.1.0]hex-6-yl]-β,β-diphenyl- (9CI) (CA INDEX NAME)

Relative stereochemistry.

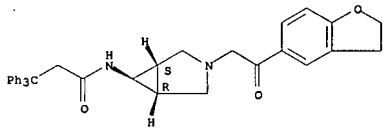
L7 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 741676-06-2 CAPLUS
CN Benzenepropanamide, N-[(1α,5α,6α)-3-[2-(2,3-dihydro-5-benzofuranyl)-2-oxoethyl]-3-azabicyclo[3.1.0]hex-6-yl]-β,β-diphenyl- (9CI) (CA INDEX NAME)

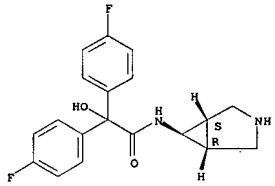
Relative stereochemistry.

Cmpd # 4
Claim 2



RN 741676-09-5 CAPLUS
CN Benzeneacetamide, N-(1α,5α,6β)-3-azabicyclo[3.1.0]hex-6-yl-4-fluoro-α-(4-fluorophenyl)-α-hydroxy- (9CI) (CA INDEX NAME)

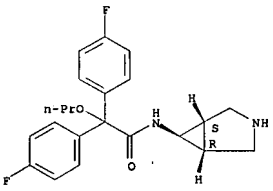
Relative stereochemistry.



RN 741676-10-8 CAPLUS
CN Benzeneacetamide, N-(1α,5α,6β)-3-azabicyclo[3.1.0]hex-6-yl-4-fluoro-α-(4-fluorophenyl)-α-propoxy- (9CI) (CA INDEX NAME)

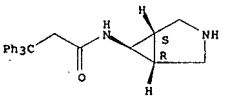
Relative stereochemistry.

L7 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



IT 741676-11-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of azabicyclohexanes as muscarinic receptor antagonists)
RN 741676-11-9 CAPLUS
CN Benzenepropanamide, N-(1α,5α,6β)-3-azabicyclo[3.1.0]hex-6-yl-β,β-diphenyl- (9CI) (CA INDEX NAME)

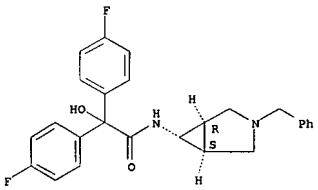
Relative stereochemistry.



IT 712355-53-8P 712355-57-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of azabicyclohexanes as muscarinic receptor antagonists)
RN 712355-53-8 CAPLUS
CN Benzeneacetamide, 4-fluoro-α-(4-fluorophenyl)-α-hydroxy-N-[(1α,5α,6α)-3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]- (9CI) (CA INDEX NAME)

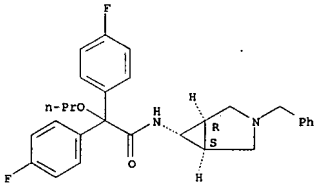
Relative stereochemistry.

L7 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 712355-57-2 CAPLUS
CN Benzeneacetamide, 4-fluoro-α-(4-fluorophenyl)-N-[(1α,5α,6α)-3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]-α-propoxy- (9CI) (CA INDEX NAME)

Relative stereochemistry.

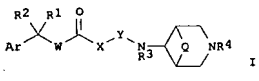


L7 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:648506 CAPLUS
DOCUMENT NUMBER: 141:190686
TITLE: Preparation of 3,6-disubstituted azabicyclohexanes as muscarinic receptor antagonists
INVENTOR(S): Mehta, Anita; Silamkoti, Arundutt V.; Kumar, Naresh; Gupta, Jang Bahadur
PATENT ASSIGNEE(S): Ranbaxy Laboratories Limited, India
SOURCE: PCT Int. Appl., 115 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004067510	A1	20040812	WO 2003-IB256	20030128
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003202727	A1	20040823	AU 2003-202727	20030128
EP 1590325	A1	20051102	EP 2003-701638	20030128
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2006247225	A1	20061102	US 2005-543585	20050727
PRIORITY APPLN. INFO.:			WO 2003-IB256 A	20030128

OTHER SOURCE(S): CASREACT 141:190686; MARPAT 141:190686
GI

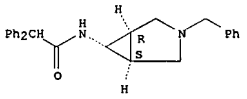


I

AB Title compds. [I; Ar = (substituted) aryl, heteroaryl; R1 = H, OH, HOCH2, alkyl, amino, alkoxy, cycloalkyl, carbamoyl, halo, aryl; R2 = alkyl, cycloalkyl, cycloalkenyl, (substituted) aryl, heteroaryl; W = (CH2)p; p = 0, 1; X = O, S, NR, null; Y = CHR5CO; R5 = H, Me, (CH2)q; q = 0-4; Q = (CH2)m; m = 0-2; R3 = H, alkyl, CO2CMe3; R4 = (unsatd.) (substituted) aliphatyl], were prepared Thus, 5-bromo-4-methylpent-3-ene, (1α,5α,6α)-6-tert-butoxycarbonylamino-3-azabicyclo[3.1.0]hexane, and K2CO3 were refluxed 5 h in MeCN to give (1α,5α,6α)-N-3-(4-methyl-3-pentenyl)-6-tert-butoxycarbonylamino-3-azabicyclo[3.1.0]hexane. This was treated with aqueous

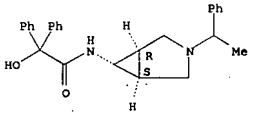
L7 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
HCl in EtOAc at 0° to give (1α,5α,6α)-N-3-(4-methyl-3-pentenyl)-6-amino-3-azabicyclo[3.1.0]hexane. The latter was stirred with 2-hydroxy-2-cyclopentyl-2-(4-methoxyphenyl)acetic acid, hydroxybenzotriazole, N-methylmorpholine, and EDC.HCl in DMF at 0° to room temp. to give (1α,5α,6α)-N-[3-(4-methyl-3-pentenyl)-3-azabicyclo[3.1.0]hex-6-yl]-2-hydroxy-2-cyclopentyl-2-(4-methoxyphenyl)acetamide. In a contractile assay using rat bladder strips, I showed pKB = 5.08-8.36 nM.
IT 712357-03-4P 738628-84-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of 3,6-disubstituted azabicyclohexanes as muscarinic receptor antagonists)
RN 712357-03-4 CAPLUS
CN Benzeneacetamide, α-phenyl-N-[(1α,5α,6α)-3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 738628-84-7 CAPLUS
CN Benzeneacetamide, α-hydroxy-α-phenyl-N-[(1α,5α,6α)-3-(1-phenylethyl)-3-azabicyclo[3.1.0]hex-6-yl]- (9CI) (CA INDEX NAME)

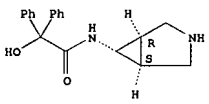
Relative stereochemistry.



IT 738629-42-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 3,6-disubstituted azabicyclohexanes as muscarinic receptor antagonists)
RN 738629-42-0 CAPLUS
CN Benzeneacetamide, N-[(1α,5α,6α)-3-azabicyclo[3.1.0]hex-6-yl]-α-hydroxy-α-phenyl- (9CI) (CA INDEX NAME)

Relative stereochemistry.

L7 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

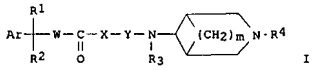


L7 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:515483 CAPLUS
DOCUMENT NUMBER: 141:71449
TITLE: Preparation of 3,6-disubstituted azabicyclo[3.1.0]hexane derivatives as muscarinic receptor antagonists
INVENTOR(S): Mehta, Anita; Silamkoti, Arundutt Visvanatham; Miriyala, Bruhaspathy; Arora, Sudershan Kumar; Srinivasulu, Boju; Mukherjee, Bireshwar; Gupta, Jang Bahadur
PATENT ASSIGNEE(S): Ranbaxy Laboratories Limited, India
SOURCE: PCT Int. Appl., 118 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004052857	A1	20040624	WO 2002-IB5220	20021210
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU 2002353286	A1	20040630	AU 2002-353286	20021210
EP 1572648	A1	20050914	EP 2002-788307	20021210
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK			
JP 2006518707	T	20060817	JP 2004-558864	20021210
US 2006217432	A1	20060928	US 2005-537851	20050608
PRIORITY APPLN. INFO.:			WO 2002-IB5220 A	20021210

OTHER SOURCE(S): CASREACT 141:71449; MARPAT 141:71449
GI



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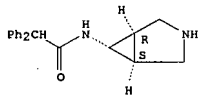
10/537857
Pat 7232835

AB Title compds. I (Ar = aryl, heteroaryl, etc.; R1cycloalkyl, cycloalkenyl, aryl, heteroaryl, etc.; R2 = H, OH, amino, alkoxy, alkenyloxy, alkynyloxy, carbamoyl, halo; W = (CH2)p; p = 0, 1; X = O, S, amino, no atom; Y = (CHR5)qCO, R5 = H, Me; (CH2)q; q = 0-4; m = 0-2; R3 = H, alkyl, CO2Bu-t; R4 = H, alkyl, etc.) and their pharmaceutically acceptable salts are prepd. The compds. of this invention can function as muscarinic receptor antagonists, and can be used for the treatment of various diseases of the respiratory, urinary and gastrointestinal systems mediated through muscarinic receptors. The invention also relates to pharmaceutical compns. contg. the compds. of the present invention and the methods for treating the diseases mediated through muscarinic receptors.

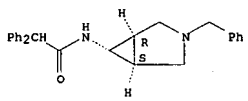
IT 712357-04-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 3,6-disubstituted azabicyclohexane derivs. as muscarinic receptor antagonists)
RN 712357-04-5 CAPLUS
CN Benzeneacetamide, N-(1α,5α,6α)-3-azabicyclo[3.1.0]hex-6-yl-α-phenyl- (9CI) (CA INDEX NAME)

Relative stereochemistry.



IT 712357-03-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 3,6-disubstituted azabicyclohexane derivs. as muscarinic receptor antagonists)
RN 712357-03-4 CAPLUS
CN Benzeneacetamide, α-phenyl-N-[(1α,5α,6α)-3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

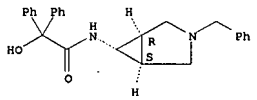


IT 712355-52-7P 712355-53-8P 712355-54-9P
712355-55-0P 712355-56-1P 712355-57-2P
712355-58-3P 712355-68-5P 712355-69-6P
712355-72-1P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 3,6-disubstituted azabicyclohexane derivs. as muscarinic receptor antagonists)

L7 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

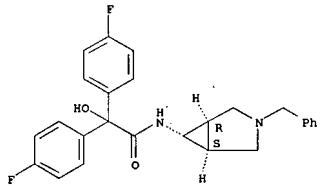
RN 712355-52-7 CAPLUS
CN Benzeneacetamide, α-hydroxy-α-phenyl-N-[(1α,5α,6α)-3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]- (9CI) (CA INDEX NAME)

Relative stereochemistry.



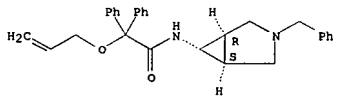
RN 712355-53-8 CAPLUS
CN Benzeneacetamide, 4-fluoro-α-(4-fluorophenyl)-α-hydroxy-N-[(1α,5α,6α)-3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]- (9CI) (CA INDEX NAME)

Relative stereochemistry.



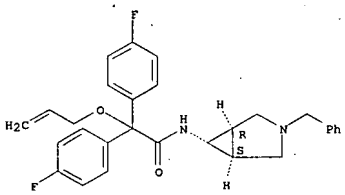
RN 712355-54-9 CAPLUS
CN Benzeneacetamide, α-phenyl-N-[(1α,5α,6α)-3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]-α-(2-propenyloxy)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



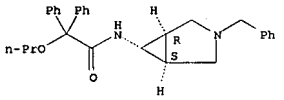
RN 712355-55-0 CAPLUS
CN Benzeneacetamide, 4-fluoro-α-(4-fluorophenyl)-N-[(1α,5α,6α)-3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]-α-(2-propenyloxy)- (9CI) (CA INDEX NAME)

L7 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
Relative stereochemistry.



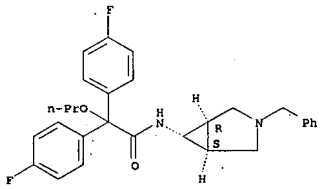
RN 712355-56-1 CAPLUS
CN Benzeneacetamide, α-phenyl-N-[(1α,5α,6α)-3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]-α-propoxy- (9CI) (CA INDEX NAME)

Relative stereochemistry.

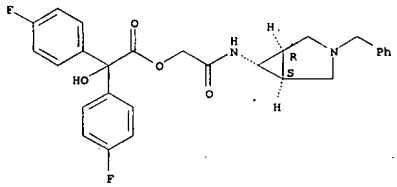


RN 712355-57-2 CAPLUS
CN Benzeneacetamide, 4-fluoro-α-(4-fluorophenyl)-N-[(1α,5α,6α)-3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]-α-propoxy- (9CI) (CA INDEX NAME)

Relative stereochemistry.

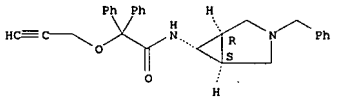


L7 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



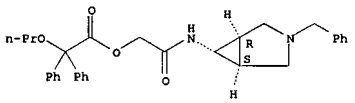
L7 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
RN 712355-58-3 CAPLUS
CN Benzeneacetamide, α-phenyl-N-[(1α,5α,6α)-3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]-α-(2-propynyloxy)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



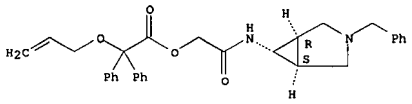
RN 712355-68-5 CAPLUS
CN Benzeneacetic acid, α-phenyl-α-propoxy-, 2-oxo-2-[[(1α,5α,6α)-3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]amino]ethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 712355-69-6 CAPLUS
CN Benzeneacetic acid, α-phenyl-α-(2-propenyloxy)-, 2-oxo-2-[[(1α,5α,6α)-3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]amino]ethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 712355-72-1 CAPLUS
CN Benzeneacetic acid, 4-fluoro-α-(4-fluorophenyl)-α-hydroxy-, 2-oxo-2-[[(1α,5α,6α)-3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]amino]ethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.